

bacteriopheophorbide and pheophorbide are. They are photosensitizers and thus claims 5, 16-17 are elected not withdrawn from consideration. Secondly because we included the possibility of using a spacer for which a specific example for searching purposes was identified does not in anyway imply that applicants have withdrawn the direct binding of the parachute structure and the therapeutic compound. The applicants clearly specified that the spacer was an option and only for completeness of response to the Election request was a specific example selected. This was reinforced in the August 7, 2002 phone conversation referenced by the examiner. Claim 7 is thus not withdrawn. Since claims 11 depends on claim 8 which is properly construed as being elected and likewise claim 13 depends on claim 12 which also is properly construed as being elected, there appears to be no basis for excluding these two claims from consideration.

The examiner has apparently changed the election agreed upon with the applicants, simply because no prior art was found. If as appears in this case that prior art may exist for a possible chemotherapeutic agent bond to a component molecule of a parachute structure, then the correct position is for examiner to challenge the novelty of claim 6 or claim 1 and any related claims.

On the basis of the examiner's election/restriction reply, he has provided evidence for allowance of all claims based on a photosensitizer, or at least those using bacteriopheophorbide or pheophorbide as the active photosensitizer. This should be so stated before switching to the alternative aspect of the invention based on chemotherapeutic species being the therapeutic compound.

The delay in replying to this action reflects in part this attorney's initial disbelief that what the examiner had done was to withdraw the specifically chosen/elected species that the applicants had made. Rereading the Detailed Action and the prior art reference after a period has confirmed to applicant that this is the only way to interpret examiner's action. We thus request that examiner issue allowances for the photosensitizer portion of all applicable claims after consideration of the responses to specific 35 USC §112 objections presented below. The 35 USC §102(b) rejections will be addressed as to the chemotherapeutic compounds since no prior art as to photosensitizers was found.

If the examiner did not mean to allow the claims based on photosensitizer compounds as the therapeutic compound, then the proper search expansion should have been to drop the optional spacer structure first do a search again. The next thing would have been to use the general porphyrin-like structure of all the named photosensitizers identified in the

claims/specification as the most general structure. Alternatively, he could have expanded the search for the use of sugars (saccharides or carbohydrates) or amino sugars as the components of the parachute structure from the glucosamine, which could have been done before expanding the photosensitizer structure. If no prior art was located at that point, then he could look for something related to claim 1 where a chemotherapeutic compound was involved. The search sequence apparently followed by the examiner has no basis in the agreement or written and oral wishes of the applicants as expressed by their representative, the attorney whose signature appears on all correspondence with the Patent Office.

In light of the extensive time and thought spent preparing the election replies and in phone conversations, it is particularly disappointing that the examiner has capriciously or unwittingly chosen a search protocol that is the 180-degrees away from applicant's indicated choice.

As to the specific objections raised by the examiner, most of the questions raised in the §112 rejections are indeed described/explained in the specification. For example, the defined distance (within the cell) from a cell's membrane is described in some detail on page 6 line 22 through page 7 line 7, and page 5 lines 16-20 of the Specification. It is tied up with the description of the 'defined action diameter' of the parachute structure on these same pages, in Figure 1 and its description page 7 lines 22-26. In spite of this, to formally answer these rejections we have amended claims 1 and 2 to reflect that one skilled in the art would preselect the desired distance from the interior membrane wall of the target cell and the action diameter of the parachute structure to obtain the desired effect on the cells when they are treated with the chosen therapeutic. Claims 8, 12, and 17 have been amended to reflect the examiner's §112 concerns and suggestion. Claim 16 has 'said membrane' not 'said member' in it and this properly anteceded by the material in claim 1 upon which claim 5 depends. Claim 4 was modified to properly reflect the original intention of the as filed claim, about which further comments follow below.

As pointed out in the specification, page 5 line 28 through page 6 line 2, oligomers of sugar have specific attachment points to cell selectins, and therefore do not need additional molecular structures to target a specific tumor tissue.

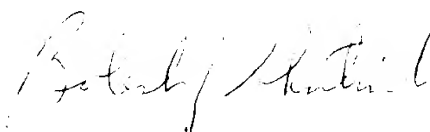
As to the prior art article under which the examiner has indicated most of the claims could be considered as being anticipated, this article, as indicated by the examiner, provides "a complex of glucosamine bonded to an anti-tumor compound through a peptide linker." A glucosamine is not the same as a di-glucosamine which can act as a 'parachute structure' along with the

branching unit. The concept of the parachute structure which can regulate to what distance into a cell an active therapeutic compound can enter, is not only not taught by the reference, but also is not implied. The disclosed article teachings do not resemble the present invention except in a most cursory way. The common use of "complex", "glucosamine", and a chemotherapeutic agent does not reveal any of the specific critical aspects of the present invention. Most basically there is no teaching why a minimum of two glucosamines (monomeric or oligomeric sugars) is desirable. The need for nor use of a 'parachute structure', as noted above, is neither taught nor suggested. A mere unit of a glucosamine does not read on the parachute structure nor on the action diameter feature which arises from the structure of the branching unit and the hydrophilic moieties attached to it. Thus there is no evidence of anticipation or obviousness for the invention even when the therapeutic compound of claim 1 is selected as in claim 6 to be a chemotherapeutic compound. No evidence of prior art for the originally elected photosensitizer-type therapeutic was found by examiner, thus all claims as amended for formality corrections should be allowable.

With these remarks it is believed that the disclosure and claims are now in condition for allowance. Consideration is respectfully requested. An early and favorable response is earnestly solicited. Thank you.

Respectfully submitted,

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What is claimed is:

1. A complex for delivery and application of drugs to cell membranes more specifically at [or a defined] a preselected distance from said [the]membrane within cells comprising:
 - at least one parachute structure, having a preselected action diameter; and
 - at least one therapeutic compound, which is selected from the group consisting of a photosensitizer and a chemotherapeutic compound.
2. A complex according to claim 1, wherein said parachute structure comprises hydrophilic moieties, [and] said [hydrophilic moieties have] parachute structure has a preselected [defined] action diameter, and wherein said action diameter [can be achieved by] is defined by the structure of a branching unit to which said hydrophilic moieties are bound and the length and structure of said hydrophilic moieties.
3. A complex according to claim 2, wherein said hydrophilic moieties are glucosamine molecules attached to said branching unit.
4. A complex according to claim 2, wherein said hydrophilic moieties are [selected from a group consisting of] sugar monomers, or [and] sugar oligomers which have specific attachment points to cell selectins [on specific cells] so that the complex is targeted to said [specific] cells.
5. A complex according to claim 1, wherein said therapeutic compound is a photosensitizer.
6. A complex according to claim 1, wherein said therapeutic compound is a chemotherapeutic drug.
7. A complex according to claim 1, wherein said parachute structure is directly bound to said therapeutic compound.
8. A complex according to claim 1, wherein said parachute structure is connected with said therapeutic compound by a spacer, and wherein said spacer [type and number of spacer used] defines the distance of said therapeutic agent to a cell's interior membrane surface [cell membranes] or its localization within the cell.
9. Cancelled


10. Cancelled
11. A complex according to claim 8, wherein using different numbers and types of said spacer to connect said therapeutic compound and said parachute structure delivers said complex into subcellular compartments at a defined distance from a surface of said subcellular compartments.
12. A complex according to claim [1] 2, wherein said parachute structures [are modified with signals] have at least one targeting species bound along said hydrophilic moieties' length to target [for targeting] said complex to a [defined] preselected tissue/cell type in an organism.
13. A complex according to claim 12, wherein said signals contain bridging structures like a Biotin-Avidin system.
14. A complex according to claim 1, wherein said complex can be used for destruction of cells, and wherein said cells are prokaryotic.
15. A complex according to claim 1, wherein said complex can be used for destruction of cells, and wherein said cells are eukaryotic.
16. A complex according to claim 5, wherein said photosensitizer is positioned close to said membrane during time of activation to render said photosensitizer more effective compared to a similar photosensitizer without said parachute structure.
17. A method for the selective destruction of [eukaryotic/prokaryotic] eukaryotic or prokaryotic cells comprising the steps of:
 - a. administering a complex to a region wherein said complex contains at least one parachute structure and at least one photosensitizer;
 - b. waiting for a pretreatment time interval to allow said complex to selectively localize at a defined position with respect to a cell membrane; and
 - I c. irradiating said region for a defined treatment time interval and intensity to activate said photosensitizer; wherein said treatment time interval and intensity are sufficient to achieve selective destruction of desired cells.
18. A complex according to claim 2, wherein said hydrophilic moieties are sugar residues.

19. A complex according to claim 8, wherein said spacer is selected from a group consisting of β -aminoacids, γ -amino butyric acid and poly-aminoacids.
20. A complex according to claim 19, wherein said spacer is selected from a group consisting of an aliphatic molecule, an aromatic molecule, a heterocyclic molecule, and an amino acid sequence.
21. A complex according to claim 20, wherein said amino acid sequence has an enzyme cleavable breaking point.
22. A complex according to claim 14, wherein said prokaryotic cells are bacteria.
23. A complex according to claim 15, wherein eukaryotic cells are human/animal cells.

What is claimed is:

1. A complex for delivery and application of drugs to cell membranes more specifically at a preselected distance from said membrane within cells comprising:
at least one parachute structure, having a preselected action diameter; and
at least one therapeutic compound, which is selected from the group consisting of
a photosensitizer and a chemotherapeutic compound.
2. A complex according to claim 1, wherein said parachute structure comprises hydrophilic moieties, said parachute structure has a preselected action diameter, and wherein said action diameter is defined by the structure of a branching unit to which said hydrophilic moieties are bound and the length and structure of said hydrophilic moieties.
3. A complex according to claim 2, wherein said hydrophilic moieties are glucosamine molecules attached to said branching unit.
4. A complex according to claim 2, wherein said hydrophilic moieties are sugar monomers, or sugar oligomers which have specific attachment points to cell selectins so that the complex is targeted to said cells.
5. A complex according to claim 1, wherein said therapeutic compound is a photosensitizer.
6. A complex according to claim 1, wherein said therapeutic compound is a chemotherapeutic drug.
7. A complex according to claim 1, wherein said parachute structure is directly bound to said therapeutic compound.
8. A complex according to claim 1, wherein said parachute structure is connected with said therapeutic compound by a spacer, and wherein said spacer defines the distance of said therapeutic agent to a cell's interior membrane surface or its localization within the cell.
9. Cancelled
10. Cancelled
11. A complex according to claim 8, wherein using different numbers and types of said spacer to connect said therapeutic compound and said parachute structure delivers

said complex into subcellular compartments at a defined distance from a surface of said subcellular compartments.

 12. A complex according to claim 2, wherein said parachute structures have at least one targeting species bound along said hydrophilic moieties' length to target said complex to a preselected tissue/cell type in an organism.


13. A complex according to claim 12, wherein said signals contain bridging structures like a Biotin-Avidin system.

14. A complex according to claim 1, wherein said complex can be used for destruction of cells, and wherein said cells are prokaryotic.

15. A complex according to claim 1, wherein said complex can be used for destruction of cells, and wherein said cells are eukaryotic.

16. A complex according to claim 5, wherein said photosensitizer is positioned close to said membrane during time of activation to render said photosensitizer more effective compared to a similar photosensitizer without said parachute structure.

17. A method for the selective destruction of eukaryotic or prokaryotic cells comprising the steps of:

-  a. administering a complex to a region wherein said complex contains at least one parachute structure and at least one photosensitizer;
- b. waiting for a pretreatment time interval to allow said complex to selectively localize at a defined position with respect to a cell membrane; and
- c. irradiating said region for a defined treatment time interval and intensity to activate said photosensitizer; wherein said treatment time interval and intensity are sufficient to achieve selective destruction of desired cells.

18. A complex according to claim 2, wherein said hydrophilic moieties are sugar residues.

19. A complex according to claim 8, wherein said spacer is selected from a group consisting of β -aminoacids, γ -amino butyric acid and poly-aminoacids.

20. A complex according to claim 19, wherein said spacer is selected from a group consisting of an aliphatic molecule, an aromatic molecule, a heterocyclic molecule, and an amino acid sequence.

21. A complex according to claim 20, wherein said amino acid sequence has an enzyme cleavable breaking point.
22. A complex according to claim 14, wherein said prokaryotic cells are bacteria.
23. A complex according to claim 15, wherein eukaryotic cells are human/animal cells.